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Number 1

IRRADIATION PNEUMONITIS in the TREATMENT OF CARCINOMA OF THE BREAST

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In the course of radiating lesions associated with the chest wall, it is at times impossible to prevent irradiation of pulmonary tissue. Irradiation of the subjacent pulmonary tissue occurs in treating carcinoma of the breast, following which pulmonary abnormalities may be observed both radiologically and clinically. This paper is an evaluation of these changes in terms of incidence, correlated factors, and morbidity.

Even before 1920 roentgenographic changes were observed in the chest following irradiation, but these were usually ascribed to local or metastatic extension of tumour. Frequently, on the basis of this diagnosis, these findings were interpreted as an indication for further roentgen therapy. Second and third "courses of treatment" were given, often with dire consequences to the patient — even death.

Evans and Leucutia⁹, in 1925, described two types of lung changes following pulmonary irradiation, namely early and late. The early consisted of "pulmonary infiltrations" coincident with clinical signs and symptoms of dry cough and dyspnea on exertion. The roentgen findings occurred three weeks following treatment and regressed in six to nine months (if no further radiation was given), or went on to "late" changes of fibrosis and atelectasis.

Desjardins⁷ (1926) gave an account of the symptomatology and signs of acute radiation pneumonitis, consisting of cough, often paroxysmal, and distressing shortness of breath, occasionally fever, weakness "proportionate to the degree of dyspnea and cardiac embarrassment", haemoptysis rarely, and commonly an increase in heart rate. The acute phase is said to have subsided in one to three weeks, with dyspnea and cough persisting for weeks or months.

Freid and Goldberg¹² (1940) reported on 18 cases receiving pulmonary irradiation, 3 of whom developed pulmonary insufficiency and right heart failure, and died. These were not breast cancers and had received whole chest irradiation.

often in several "courses" over a period of years. The principal pathological changes at autopsy were abundant fibrotic reaction, bronchiectasis, atherosclerosis and thromboses of pulmonary arteries. There was also hypertrophy and/or dilatation of the right atrium and ventricle. They speculated that the right ventricular failure may have been due to alterations in the pulmonary vascular bed as well as changes in the position of the heart and great vessels. It is now felt that alterations in position of the heart and great vessels per se probably have little, if anything, to do with the development of cor pulmonale and right ventricular failure. 10,11

More recently, with the advent of higher energy apparatus and the discovery of the antiinflammatory steroid hormones, interest in the subject of radiation pneumonitis has been revived. Articles have been published describing severe and even fatal pulmonary reactions following high doses of radiation to the lungs, 4.12.18.22 and others are concerned with the prevention and reversal of chronic lung disease (due to radiation or otherwise) by the use of ACTH or adrenal steroids. 3.5.6.13,16.18

Most of the reports on radiation changes have been concerned with the treatment of hilar or mediastinal lesions, such as Hodgkin's disease involving mediastinal nodes, and particularly carcinoma of the oesophagus. The presence of pre-existing disease and the possibility of persistent disease tends to confuse the lung picture clinically and radiologically in these conditions. We have therefore confined ourselves to similar changes occurring as a result of treating carcinoma of the breast by irradiation. A review of carcinoma of the breast at the Montreal General Hospital has been carried out, with particular attention to those receiving radiation. The five years from 1953 to 1957 inclusive have been covered because only in 1953 did radiation first play a substantial part in treatment of carcinoma of the breast at this Hospital. In that year also, intensive pre-operative irradiation was initiated in later stages of breast carcinoma.

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Material

In these five years 491 new cases of breast carcinoma were seen. Of these, 255 received radiation therapy, 94 with quadrate fields as primary treatment, and 91 post-operative radiation to immediate areas of lymphatic drainage. The other 70 received irradiation for metastases to other areas (see Table 1).

Table I

M.G.H.

CA. BREAST, 1953-1957

Total	491
Rec'd Radiation	255
Quadrate	94
Lymph Node Areas	91
Other Areas	70

Radiation Techniques

The quadrate radiation consists of four fields directed tangentially to the breast and immediate lymphatic areas, opposing medial and lateral fields which include the internal mammary chain of lymph nodes and whole axilla in each beam, as well as the involved breast, and opposing supero-inferior and infero-superior fields, each of these including the whole axilla in the beam as well as the breast. For each treatment, bolus is used so that a solid block including the internal mammary nodes, axilla, breast, and intervening chest wall, is irradiated to a fairly uniform dose. This necessarily includes lung tissue (Figure 5). For all but the extremes of body build a field 20 cm. in length suffices for the medial and lateral fields, and a field 15 cm. in length for the other two. All fields are 10 cm. in width. This large block of tissue is treated to tolerance. There is wide variation in the dose tolerated. Usually the whole procedure is carried out with 250 KVP radiation, HVL 2.4 mm. copper, FSD 50 cm., and takes from ten to twelve weeks, treating five times weekly.

The post-operative irradiation (which is never given to patients who have had pre-operative irradiation) consists of three direct fields: an AP mediastinal field approximately 9 x 18 cm., an AP supraclavicular field approximately 8 x 16 cm., and a direct axillary field approximately 10 x 10 cm. (with the arm abducted). The axillary field is so arranged as to be perpendicular to the skin but tangential to the apex of the lung. The exact measurements of the various fields vary with the dimensions of the patient. The hila of both lungs are necessarily included in the AP mediastinal field, but the depth dose at the midpoint of the hilum is of the order of 2000 r to 2500 r. A variable portion of the apex of the lung is included in both the supraclavicular and axillary fields and necessarily receives a much higher dose. A combination of 250 KVP and Cobalt 60 irradiation is used, the Cobalt 60 being used since 1955. The overall time of treatment is usually six to seven weeks. The dose 3 cm. below the skin in the retrosternal area is approximately 4600 r, in the axillary apex 6800-7400 r.

Diagnosis of Radiation Pneumonitis

Diagnosis of radiation pneumonitis is based on:

(1) Clinical signs and symptoms:

- (a) Fever low-grade; usually no higher than 102° F.
- (b) Prostration.
- (c) Dyspnea on exertion.
- (d) Cough non-productive.
- (e) Tachycardia often out of proportion to the fever.

(2) Roentgen findings:

- (a) Infiltration:
 - (i) Coarse reticulation which may be faint and difficult to appreciate,
 - (ii) Patchy, often resembling a localized pulmonary oedema.
- (b) Contraction (or atelectasis) of the involved lung.
- (c) "Tenting" of the dome of the dia-
- (d) Absence of pleural effusion (although localized pleural thickening may
- (e) Correlation of the site of radiation and the distribution of the pulmonary pathology.

The clinical signs and symptoms accompanied by roentgenographic evidence of lung infiltration, usually without atelectasis initially, typically occur from one to four weeks after the end of treatment. The above factors will be discussed after reviewing the results of this series.

Observations

Chest films were made on all patients before, during, and after treatment. An attempt was made also to have films one to two weeks, one month, and three months following treatment, and subsequently at three to six month intervals for at least one year. This was done as an investigative procedure. Nearly all the patients had no signs or symptoms referable to the respiratory

Of the 94 patients receiving quadrate therapy, 69 had follow-up chest X-rays over a sufficient period of time to diagnose or rule out pulmonary disease secondary to irradiation. 27 patients did not develop roentgen changes at any time up to

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one to four years following treatment. The remainder (42 patients) had changes in the lungs which were attributed only to the direct or indirect effects of radiation. These varied considerably in extent and accordingly were classified into three groups: minimal, moderate, and

Those were classified as minimal in whom the infiltration was restricted to the anterior portions of the upper lobe (and right middle lobe or lingula), with slight or no signs of contraction of the lung (Figure 1). The roentgen signs are often manifest only in the lateral projection and could go completely unrecognized if attention were directed solely to the PA film. A very faint reticulation of most of the upper lobe was also classified as minimal.

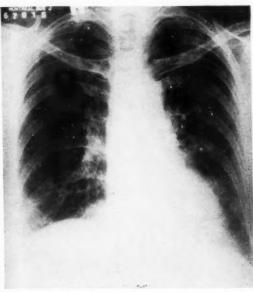


Figure 1 - Minimal Reaction - Mrs. I. D., 69 yrs; quadrate radiation to left chest to a dose of 7000 r in 73 days (preceded by simple mastectomy). This X-ray was made 2 days before the completion of treatment, at which time there were no symptoms referable to the lungs. Note the "coarse reticulation" pattern.

Moderate changes consisted of involvement of most of the upper lobe (and right middle lobe or lingula) in an obvious infiltrative process, often accompanied by signs of some atelectasis (Figure 2).

Marked changes consisted of extensive infiltration and contraction of most of the upper lobe and rarely slight involvement of the lower lobe as well (Figures 3a, 3b, 4a). Tenting of the dome of the diaphragm was a common finding.

The average dose to patients with no lung changes (on X-ray) was 5600 r tumour dose in 67 days, and the range was 2000 r tumour dose in 43 days to 7800 r in 102 days. The average dose to the patients in whom minimal lung changes occurred was 6800 r tumour dose in 76 days, and the range 3400 r in 53 days to 8500 r in 78 days. For moderate changes the average dose was 6900 r tumour dose in 71 days - range 5100 r in 50 days to 8800 r in 89 days (Table II).

Table II

Quadrate Radiation Lung Reaction & Dose

Lung Changes (X-ray)	Av. T.D.	Dose Range	Aver. Time	No.
None	5600 r	2000-7800 г	67 da.	27
Minimal	6800	3400-8500	76	14
Moderate	6900	5100-8800	71	6
Marked	6600	3800-8600	79	22
	Total	69 patients		

Marked lung changes occurred at an average dose of 6600 r tumour dose in 79 days - range 3800 r in 32 days to 8600 r in 95 days.

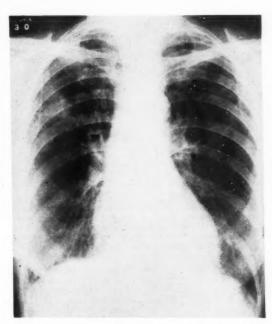


Figure 2 - Moderate Reaction - Mrs. J. M., 79 yrs; quadrate radiation to right chest to a dose of 6500 r in 88 days. Treatment was terminated because she developed signs and symptoms of radiation pneumonitis. A film made at the onset of symptoms showed essentially the same findings as the above film, made 10 days later. Note the scattered areas of consolidation and/or segmental atelectasis in the right lung. The left lung is unchanged since the beginning of treatment.

Of the 91 patients receiving post-operative roentgen therapy, 46 had sufficient follow-up examinations to be considered. Of these, 17 had lung changes, 9 with minimal infiltration in the

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apex of the upper lobe, and 8 with moderate infiltration and some roentgen signs of partial atelectasis of the upper lobe, and apical pleural thickening. The degree and extent of radiation changes were much less than similarly classified cases receiving quadrate therapy. Tenting of the diaphragm rarely occurred in the post-operative group, and the antero-inferior portions of the upper lobe (and right middle lobe and lingula) were never involved (Figure 6). The average dose to the lung near the axillary apex in patients with lung reactions was 6500 r in 49 days, and those without reactions 6600 r in 48 days. No hilar changes occurred in these cases.



Figure 3 (a) — Moderate to Marked Reaction — Mrs. J. B., 63 yrs; quadrate radiation to left chest to a dose of 7700 r in 80 days. X-ray changes first appeared 4 weeks after treatment and progressed to this extent by 8 weeks. At no time did the patient experience signs or symptoms referable to the lungs.

Of considerable importance is the fact that the clinical syndrome of acute radiation pneumonitis was recognized in only 4 patients after quadrate therapy and in no case after postoperative therapy. In 2 of the 4 cases radiation was discontinued because the patients developed symptoms of pneumonitis and were too sick to be treated (they were in the last week of treatment). The symptoms in such patients are relatively acute in onset but may be preceded by a dry cough for a few days or weeks, and also mild malaise, though the latter is difficult to distinguish from the usual "tiredness" of the patient towards the end of long-term radiation.

The time of appearance of the lung changes will be considered in terms of interval from the end of treatment and interval from the beginning of treatment, since the duration of treatment in our cases may differ from those of others. In quadrate therapy the average time when films showed changes was 10 weeks from the end of treatment and approximately 20 weeks from the beginning. In post-operative cases most showed changes by seven weeks from the end of treatment or fifteen weeks from the beginning.

Pleural effusion was strikingly absent in our series. In no case did a basal pleural effusion occur which was attributable to irradiation. Localized pleural thickening occurred in some cases, and is quite typical in the lung after post-operative radiation.



Figure 3 (b) — Same examination as in 3 (a) to illustrate the anterior location of the X-ray changes, as is the case in all patients receiving quadrate radiation.

In 44 cases of quadrate therapy, information was obtainable as to the subsequent course of the tumour either by proven clinical local recurrence, subsequent mastectomy, or autopsy study. There were 6 local recurrences, 27 cases in which recognizable tumour was found by microscopic examination, with no evidence of regrowth of tumour, and 11 cases $(25\%_0)$ in which no tumour could be found in multiple sections of the breast All these cases had had pathologically proven carcinoma. The average dose in cases of local

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recurrence was 4800 r (range 3000-6500 r). The average dose in which "sterilization" of the breast occurred was 7000 r (range 6000-8800 r). The overall average dose for the group was 6000 r.

In those cases where the lung changes were incidental findings on X-ray examination, resolution was infrequent. Of 59 cases, only 5 (8.5%) showed partial resolution. None showed complete resolution. Of the 4 patients with the full syndrome of pneumonitis, treated with steroids, none showed regression of lung changes radiologically.

stage, but also in the stage of "contraction". This latter, then, does not necessarily represent fibrosis and contraction of scar tissue in the lung. Another fact which prevents simplification is that while in many cases one phase follows the other, in many others the stage of infiltration never occurs, the first changes seen being those of loss of lung volume and "scarring". It is true that in some (perhaps the majority) of these cases the acute "infiltrative" stage may have been missed due to insufficient followup films, but in some cases weekly films were done during and after treatment and it was shown that the infiltrative phase never did occur.

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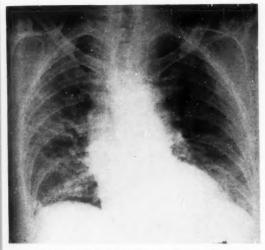


Figure 4 (a) — Marked Reaction — Mrs. L. M., 67 yrs; quadrate radiation to right chest to a dose of 6000 r in 78 days. Chest X-ray made at the time when treatment was terminated because of the development of severe clinical signs and symptoms of radiation pneumonitis. Note extensive infiltration with some loss of volume, but little tendency to consolidation.

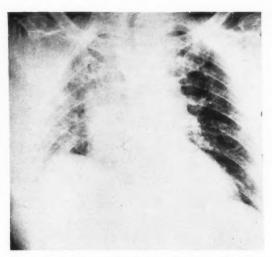


Figure 4 (b) — Same patient as in 4 (a), 18 months after treatment (asymptomatic for some 16 months) showing persistent marked loss of volume of the right lung anteriorly. On physical examination there was dullness to percussion anteriorly, with hyperresonance posteriorly on the right.

Discussion-Pathology

It becomes apparent on review of cases such as these that there are two types of change that occur in the chest films of patients with radiation pneumonitis. One is an infiltrative process in which the loss of lung volume is minor, and the other is one in which the major change is that of lung "scarring" and contraction. The temptation is great to simplify the situation and say that the appearance of infiltration represents the initial phase of vascular congestion, oedema, and inflammatory infiltration that has been reported by Evans and Leucutia,9 and that this is followed by organization, fibrosis and contraction of the lung, as one might expect in any pneumonitis which does not heal by resolution. However, the fact is that resolution, though uncommon in our series, can and does occur spontaneously not only in the "infiltrative"

Furthermore, the experimental work of Berdjis and Brown^{3,5} on the effects of radiation on the rat lung (and the influence of cortisone upon them), showed atrophy and squamous metaplasia of bronchial epithelium and atelectasis of the lung, with varying degrees of fibrosis. These changes appeared early and those of oedema and congestion, though present, were apparently completely masked. Still others report the occurrence of focal emphysema and atelectasis3,22 and hyaline membrane formation in alveoli. 9,19,22 The microscopic pathology is not specific. Warren and Spencer reviewed the lung sections in 1060 consecutive autopsies without any knowledge of their history and found 7 cases of "typical radiation pneumonitis"; 4 of these had had irradiation, 3 had had none. The "typical" findings also occur in chronic nonspecific interstitial pneumonitis, influenzal pneumonia, the early stages of chemical pneumonia and the pneumonic form of bubonic plague.

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mation purse of all recury study. In which roscopic bowth of tumour threast. proven of local It can be seen that the lung changes produced by irradiation are many and varied. It is not our purpose to discuss the pathology of the changes, which have been fully reported by others. 7.8,9,19,20,22 Suffice it to say that two groups of changes probably occur which are most important from the functional and roentgenological point of view, one consisting of capillary engorgement, thickening of alveolar walls and oedema of alveolar spaces with varying degrees of diapedesis of red blood cells, and leukocytic infiltration, and the other consisting of varying degrees of focal emphysema and atelectasis possibly as the result of changes in the bronchial and bronchiolar walls.

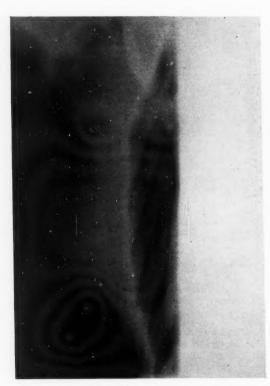


Figure 5 - Localizing film of a medial field (without bolus) to illustrate the inclusion of the antero-lateral segments of the lung in the treatment beam.

Radiology

From the diversified pathology described, it is surprising that the roentgenographic manifestations are usually so typical. Little is added in trying to simplify them further by imposing the temporal sequence of: radiation, infiltration, fibrosis and contraction.

There are certain other features about the lung changes which are important in the diagnosis of radiation pneumonitis:

- 1. History It must be verified that the patient did receive irradiation.
- 2. Site The pneumonitis is a local response of the lung to local irradiation, therefore the involved area of lung must be within the treatment field.
- 3. Dose Here there is great individual variation but, as we have seen, the average dose resulting in radiologically identifiable pulmonary changes ranged from 6600 r in 79 days to 6900 r in 71 days (in quadrate radiation). A dose as low as 3400 r in 53 days produced changes in one patient, while in another 7800 r in 102 days produced none. The average dose in patients showing no pulmonary changes is significantly lower than that in patients who do, yet there is no correlation between the severity of the lung changes and the dose when a reaction does occur. In no case of mediastinal irradiation in which the depth dose ranged from 2000-2500 r in 6 to 8 weeks did recognizable changes occur. Thus, if there is a critical level below which pneumonitis does not occur, it probably lies somewhere between 2500 and 3400 r in approximately 7 weeks.
 - 4. Time Interval The lung changes tend to appear within the first 2 to 3 months following treatment. In some cases the changes are not demonstrated until much later, but this is usually due to a long time-gap during which routine films are not made.

The clinical manifestations of pneumonitis appeared just before or within a few weeks of the completion of radiation therapy. The pulmonary changes by X-ray also appeared early, being present at the onset of symptoms and at this time were minimal or moderate, but progressed even as the patient began to improve clinically.

Conflicting reports have appeared regarding pleural effusion in radiation pneumonitis. Whitfield et al22 reported pleural effusion in their fatal case. Ross17 states that pleural effusion, particularly at the lung base, is a common finding. Bate and Guttman² noted in 7 of 35 patients who had lung changes following irradiation for carcinoma of the breast, moderate pleural effusions requiring thoracentesis. On the other hand, Brown⁵ (in experimental studies on the rat lung (giving 3000 r in a single dose)) noted only slight pleural fibrosis, and no pleural effusions, except in animals dying of superimposed infective pneumonia. Evans and Leucutia9 describe the pleural changes as fibrosis only, without effusion. Warren and Gates19, in an

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excellent and thorough description of the pathology of the various elements of the lung in response to fractionated irradiation (both experimental and clinical study), concluded that the pleura is the least sensitive of all, reacting last and least. The changes consist in swelling of mesothelial cells, hyalinization and slight oedema of the underlying connective tissue, but no pleural effusion.



Figure 6 - Reaction to Post-Operative Radiation Mrs. J. M., dose 7000 r in 51 days. This film was made one year following treatment. The site and appearance of the changes are typical, though much more marked than usually seen following this type of treatment. Note the absence of changes in the hilar area, and mid and lower lung.

The findings in this series are in keeping with these experimental and clinical pathological studies. In only 1 of 59 cases of pneumonitis did basal pleural effusion occur. This was bilateral and demonstrated 2 days ante mortem, 7 months after the end of treatment. Unfortunately, no autopsy was obtained in this patient, but it is almost certain that the effusion represented a terminal event not due to irradiation. Death in this case was not due to lung changes as the patient had no symptoms referable to pneumonitis.

What one interprets radiologically as "pleural thickening" is a very common occurrence, though, and in fact, is typical, particularly at the lung apex after post-operative irradiation. No one can deny localized effusion in such cases on radiological grounds, but it almost invariably proves to be parenchymal fibrosis and pleural thickening with no fluid. Six such cases in our series have since come to autopsy, and neither fluid nor tumour was demonstrated at the site of pleural thickening in any of them. When a patient who has had pulmonary radiation presents with a basal pleural effusion in addition to parenchymal changes, the most likely diagnosis is carcinomatosis. Infectious pneumonia, congestive failure, or other causes of effusion should be considered, but radiation as a cause of effusion is highly improbable. Certainly if the lungs are clear in the presence of effusion, radiation is not the explanation.

While it is not our purpose to discuss cure rates, the local cure of carcinoma is significantly greater using a "treat to tolerance" technique. The actual results obtained in the Montreal General Hospital will be reported in a subsequent paper, but we believe that the improved results justify every effort to bring this large area of tissue to as high a dose as possible. In order to irradiate this large mass of tissue en bloc, using conventional apparatus, it has been found necessary to carry out prolonged fractionation, which the patient tolerates better and allows the therapist to judge better the "tolerance dose" for the individual.

Syndrome of Radiation Pneumonitis

A small proportion of patients present with symptoms which are quite typical and usually offer little problem in diagnosis. Characteristically, at or near the end of treatment the patient begins to complain of feeling unwell. There is a low-grade fever, malaise, and prostration out of proportion to the fever. Cough is present and may be troublesome. Dyspnoea of radiation pneumonitis following mammary irradiation is less marked than in the case of those diseases involving hilar radiation.

Pneumonitis with symptoms did not occur in our patients given post-operative irradiation. From this it is concluded that the severity of lung reaction is in part related to the volume of lung irradiated.

Though the average mild clinical case is probably self-limiting, prompt relief is obtained by cortisone or ACTH. Dosage has not been standardized but most cases are dramatically relieved in one to three days at a cortisone dosage of 100-200 mg. per day. As improvement occurs, the dose can be reduced. Two to three weeks of treatment usually suffices. The patient can reliably state when the dose is being too rapidly reduced.

Case Report

Mrs. L. M., was a 67 year old woman who received 6000 r by quadrate therapy in 11 weeks (March 25th, June 11th, 1954) for an ulcerating carcinoma of the right breast. A few days before the planned end of her treatment she became very ill with prostration, shortness of breath, cough and anorexia, and treatment had to be terminated. Four days later she developed nausea and vomiting, which subsided within a week. On admission to hospital on June 16th, 1954, she was moderately dehydrated, looked very ill, was orthopnoeic and pale, with slight cyanosis of the lips and nail beds. On physical examination her temperature was 99.2° F., pulse 126 per minute, blood pressure 108/76, and respirations 24 per minute. The trachea was midline. Chest expansion was poor on the right but percussion was normal, and breath sounds were broncho-vesicular with no adventitious sounds. In the cardiovascular system the only abnormality on auscultation was an accentuation of \mathbf{P}_2 . The remainder of the physical examination was entirely normal. ECG showed left axis deviation but was unchanged from an ECG in 1950 except for sinus tachycardia. A portable X-ray of the chest revealed parenchymal infiltration without consolidation on the right, moderate in extent (see Figure 4a). Her red cell count was 3,800,000 per cu.mm., haemoglobin 11.5 gm., and white cell count 6,650 per cu.mm.

In the belief that the illness might be due to superimposed infection as well as radiation, intramuscular penicillin and streptomycin were started on admission, in addition to intravenous fluids, to correct the dehydration. The antibiotics had no effect and the temperature rose to 102° F. in the next twenty-four hours. Cortisone 25 mg. q.i.d. orally was started on June 25th, 1954. Subjective improvement occurred, but the temperature remained elevated though not as high as formerly. ACTH was started on June 26th, 25 mg. per day in a slow intravenous drip for three days, then changed to 40 mg. long-acting ACTH intramuscular daily. The clinical response to this was satisfactory. The temperature dropped the same day and remained close to normal except for a brief period when an attempt was made to reduce the dosage of ACTH. The tachycardia was slower to respond. The ACTH was continued for three months following her discharge on July 24th, 1954, in an attempt to prevent fibrosis of the lung. Follow-up chest examination eighteen months later, however, showed marked mediastinal retraction, elevation of the diaphragm, and contraction of the right upper lobe (Figure 4b). Physical examina-tion revealed dullness, decreased breath sounds and coarse rhonchi over the right chest anteriorly, with hyperresonance and bronchovesicular breath sounds posteriorly. The left lung remained normal to all examinations. The patient is alive and well at this time (January, 1958) with the physical and X-ray findings in the chest unchanged, but no symptoms referable to the chest. There is no evidence of tumour in the breast or axilla on clinical examination.

The apparent failure of cortisone in this case may have been due to a number of factors: too low a dose, insufficient clinical trial, or failure of absorption due to residual gastro-intestinal upset.

We have seen that lung reactions are more common when larger volumes of tissue are irradiated and the lung reaction tends to be more severe. However, one cannot predict from the dose administered how much the lung changes will be in the asymptomatic case. Nor can one predict from the dose or the degree of changes in the chest X-ray which patient is likely to have clinical pneumonitis. The dose in roentgens and the time of treatment in days and the degree of lung changes on X-ray examination are tabulated for the 4 patients in our

series who developed the irradiation pneumonitis syndrome (Table III). The first 2 patients (E.M. and M.S.) had doses well in excess of 8000 r and developed only minimal and moderate changes respectively, and the severity of the clinical symptoms was relatively mild. These patients did not develop their symptoms until one to two weeks after the completion of radiation therapy. The last 2 patients (L.M. and - doses of 6000 r and 6500 r respectively) developed moderate and marked lung changes. These patients were severely ill. They are the two in whom symptoms developed before the completion of therapy and who were too ill to continue treatment. Thus, where symptoms do occur there is probably some correlation between the severity of the illness, the amount of lung changes demonstrated on X-ray, and the time of appearance of the symptoms. The earlier the onset, the more severe the symptoms tend to be and the more marked the pulmonary changes are likely to be.

Table III

Radiation Pneumonitis Syndrome 4 Cases

	Dose	Time	Lung Changes (X-ray)
E.M.	8500 r	78 da	Minima!
M.S.	8800	89	Moderate
L.M.	6000	78	Marked
J.N.	6500	88	Moderate

Resolution

While there is dramatic subjective response to the corticoids, we have not seen any significant tendency towards improvement in the chest X-ray in follow-up examinations. None of the 4 symptomatic cases showed X-ray evidence of resolution on cortisone. Perhaps our dosage has been too low, or was not carried on long enough. However, it is very difficult to evaluate resolution on corticoids since spontaneous resolution, though uncommon, does occur. Experimentally, Brown⁵ and Berdjis and Brown³ showed cortisone to have some beneficial effect in animals when given before or shortly after radiation. Their radiation methods were not conventional, consisting of a single dose of 3000 r to a whole lung. There is as yet no experimental work in which radiation has been administered in a manner comparable to that used in clinical practice, nor any well controlled clinical study in which the effects of corticosteroids have been evaluated. In practice, by the time the patient develops symptoms of pneumonitis and is put on cortisone, the tissue changes have been occurring in the lung for some 2 to 4 months and are well established. Also by the time symptoms develop, roentgen evidence of disease is almost invariably present. Corticoids may delay or prevent the progression of tijectifeve

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of these changes, judging by the prompt subjective improvement and disappearance of fever. The failure of the lung fields to return to normal on roentgen examination does not mean cortisone was without effect. One should not expect or require the lungs to return to normal appearance on X-ray examination, just as one would not expect the skin to become normal. It is possible to minimize trauma to the skin and to apply bland emollient medications (or cortisone) to keep it in quite good condition. However, the damaged lung is less easily aided, and any chronic changes which tend to produce focal emphysema and atelectasis might be expected to progress to considerable degree. Atelectasis is often marked; contraction is often extreme. It does not require fibrosis to produce it (though some fibrosis is usually present), but merely a disturbance in the distribution of air in the lung during respiration. Anti-inflammatory drugs, if radiation is prolonged, may therefore inhibit or prevent further fibrotic changes, but should not be expected to result in normal-appearing lungs in every case.

One more comment should be made on resolution. In earlier times, when resolution was the usual result, the method of irradiation was quite different than it is today. Single dose treatments or treatments over periods of 1 to 2 weeks were the rule. Now the treatment extends over a period of weeks and sometimes months. Nonetheless, it is recorded in earlier literature that if lung changes occurred following a second "course of treatment" at an interval of 2 to 3 months, the alterations in the appearance of the lung tended to persist rather than clear up.9

Conclusions

- (1). With sufficient history as to the amount and distribution of radiation to the chest (and lungs) and the time interval, one can diagnose with accuracy the radiation pneumonitis syndrome.
- (2) In the more common asymptomatic case showing lung changes of typical appearance and distribution, if similar information is available, one can confidently attribute the changes to radiation effect and not to metastases. Though metastases can occur in this altered tissue, they are difficult to identify.
- (3) Localized "pleural thickening" at the periphery and in fissures is common, but a basal pleural effusion is not seen and should make one very cautious of attributing the changes solely to radiation.
- (4) The occurrence of lung changes shows poor correlation with dosage. It is more closely related to the amount of tissue irradiated. The severity of the lung changes varies with the individual.

- (5) Radiation pneumonitis should be suspected in the patient who develops cough, malaise, and shortness of breath while undergoing radiation to the lung. It must be remembered that physical signs of lung disease may be absent in radiation pneumonitis and that early roentgen changes may be very minimal and easily missed.
- (6) Though the lung roots do not receive heavy irradiation during the treatment of a primary breast lesion, the characteristics of the resulting pneumonitis must be the same. Because of the hazard of permanent pulmonary insufficiency following hilar irradiation, perhaps more attention must be paid to early signs of pneumonitis in such cases.

Summary

- (1) 255 patients receiving irradiation for carcinoma of the breast are reviewed. Of these, 94 received quadrate therapy to the breast, chest wall, axilla and anterior mediastinal lymph nodes en bloc; 91 received postoperative irradiation to the areas of lymphatic drainage alone, and 70 patients received no significant amount of irradiation to the chest.
- (2) Of 94 quadrate cases, 69 had sufficient follow-up examinations, and of these, 42 (61%) developed abnormalities in chest roentgenograms attributable to radiation alone.
- (3) Of 91 cases of post-operative irradiation, 46 had sufficient follow-up examinations, and 17 (37%) developed changes in chest roentgenograms attributable to radiation.
- (4) The average dose to patients receiving quadrate therapy resulting in lung changes was approximately 6500-7000 r in 10 to 11 weeks, the radiation including the anterolateral pulmonary segment. The average dose to patients receiving post-operative therapy was approximately 6500 r in 7 weeks to a relatively small portion of the apex of the upper lobe, and in these the changes are much less extensive and less
- (5) The average dose to patients with radiation changes in the lungs demonstrable on chest X-ray is significantly higher than the average dose to those whose lungs remain normal, but there is no statistical difference between the doses resulting in minimal, moderate, or marked lung changes respectively.
- (6) Basal pleural effusion was not seen as a radiation effect.

- (7) Even severe lung alterations are usually asymptomatic. A few patients (probably less than 4% of the whole group) developed typical signs and symptoms which responded readily to ACTH or cortisone in relatively low doses.
- (8) Spontaneous resolution of lung changes does occur but in only a small proportion of cases, and it is incomplete.

ACKNOWLEDGMENT: Dr. C. W. Fullerton, Professor of Therapeutics, McGill University, and Senior Physician, The Montreal General Hospital, provided clinical information. Dr. W. K. MacDonald, Medical Director, Schering Corporation Ltd., Montreal, made available meticorten for clinical use in the early cases of radiation pneumonitis.

To them we are indebted and wish to express our thanks for their help.

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CONTRIBUTIONS TO THE NATURAL BACKGROUND DOSE DUE TO Cs137 ARISING FROM FALLOUT

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Abstract

Measurements of the caesium activity arising from fallout have been made in some 50 Toronto residents over the last year. These measurements were made using a whole body counter in the Physics Department of the University of Toronto. The measurements are described and the radiation dose received from Cs137 compared with that arising from other sources.

Introduction

In the last few years a great deal of concern has been expressed over the ingestion by humans of radioactive materials produced in the fallout from nuclear bomb tests. Unfortunately, it is difficult to separate the concern which arises from purely scientific reasoning from that which arises from political considerations. In order to retain a proper perspective, it is essential to compare the radiation exposure resulting from fallout with that produced by natural background and by man-made sources of radiation. In this paper, measurements made of the caesium activity of 50 members of the University of Toronto will be described and the dose arising from this activity will be discussed.

Apparatus

In order to make possible the measurement of the low level radioactivity of the human body, it is necessary both to use thick shielding to cut out background effects due to cosmic radiation and local radioactivity, and to have a sensitive detector. In the University of Toronto the shielding is in the form of a room $6' \times 7' \times 5'$ with steel walls 8'' thick. During the construction of the room, measurements were made at various stages and it was found that the 8" of steel actually reduced the background by a factor of 40.

The heart of the gamma ray detecting apparatus (Figure 1) is a sodium iodide crystal 5" in diameter and 4" thick, which is connected to a 5" Du Mont photomultiplier. The pulses from the photomultiplier are amplified in a preamplifier within the room and then amplified still further before being sorted in a 100 channel pulse height analyser. It is usual to make measurements with the person in a reclining form as suggested by Figure 1. This brings the crystal into the best geometry for detecting radiation from the thorax, abdomen and legs of the person. For further details of the apparatus, reference should be made to previous papers^{6,7,8}.

Results

Typical results obtained on a normal person are shown in Figure 2 where the pulse height distribution, given in counts per 21 Key channel width for 30 minutes, is plotted against the energy of the radiation in Mev. To obtain this pulse height distribution, the person was counted for a 30 minute period and then background counted for a corresponding period, and the difference between the two spectral distributions taken to give the radiation which arose from the subject. Before making a measurement on a person, it is necessary to have the person remove all street clothes and shower carefully to get rid of any activity which might be present in the clothes or on the skin.

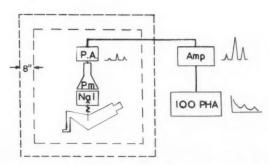


Figure 1 - Block diagram of equipment for detecting body activity.

The spectral distribution of Figure 2 shows two distinct peaks at 1.46 Mev and 0.66 Mev. The 1.46 Mev peak is due to the presence of radioactive K40 which occurs with a natural abundance of 0.0119%. It emits¹² a beta particle of energy 1.33 Mev in 89% of disintegrations. In the rest of the disintegrations, electron conversion takes place followed by a 1.46 Mev gamma ray. The peak at 0.66 Mev is due to the presence of Cs137. In 92% of the Cs137 disintegrations1, a beta particle of maximum energy 0.54 Mev is emitted leading to an excited state of Ba137. In the other 8% of the disintegrations,

a beta particle of 1.18 Mev is emitted leading to the ground state of Ba¹³⁷. The excited state loses its energy by the ejection of a 0.66 Mev gamma ray in 82.3% of the Cs disintegrations, the other 9.7% (9.7% + 82.3% = 92%) of the disintegrations resulting in conversion electrons. Before the era of nuclear fission, it is certain that human beings did not show this peak at 0.66 Mev, as Cs¹³⁷ does not occur in nature.

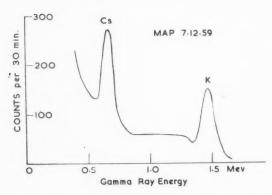


Figure 2 — Typical gamma ray spectra for a normal person measured for 30 minutes. At the time of the measurement (1959), the person contained 73 caesium units.

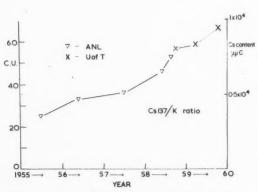


Figure 3 — Graph showing the change of Cs^{137} activity of the human body with time. On the left scale C.U. refers to the ratio of the Cs activity to the K content in $\mu\mu$ C per gram of natural K. The right-hand scale gives the total activity in $\mu\mu$ C of Cs assuming the body to contain the standard amount of K of 140 grams.

The amount of Cs within the person may be determined by comparing the area under the 0.66 Mev peak with that under the 1.46 Mev peak. From a knowledge of the amount of K in the body⁸, it is then possible to calculate the amount of Cs present in the body. In presenting results for Cs, it is usual to express the amount of Cs in $\mu\mu$ C per gram of natural K in the body, this ratio being referred to as the caesium unit

(C.U.). This unit is useful because Cs and K are distributed in the body in much the same way and the amount of K incorporated into the body depends to a certain extent on the ratio of the amount of fat to muscle and the age and sex of the individual concerned. By expressing the amount of Cs in terms of the amount of K, one removes the variation in the Cs content resulting from variations in fat, muscle, sex and age. Figure 3 shows the results of measurements of this Cs to K ratio made at the University of Toronto during 1958 and 1959. It is seen that over this period of time the Cs: K ratio has risen from about 57 to 67 C.U. Before 1958 no measurements were made in Toronto, but measurements have been made since 1955 at the Argonne National Laboratory. The results obtained in this period10 are also shown in the figure. The trend towards higher Cs content with time is evident and can be correlated to some extent with the number and types of bombs which have been tested. On the right-hand side of the diagram the amount of Cs, expressed in μμC per person, is shown. This was obtained from the C.U. ratio assuming that each person contained 140 gm of K, the amount defined as being present in the standard man3. It is seen that at the present time the average person contains about 8.4 x $10^3 \mu\mu$ C of Cs¹³⁷.

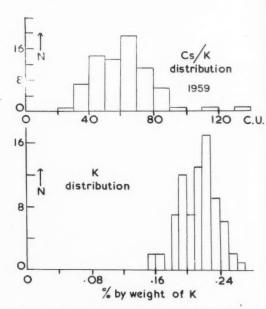


Figure 4 — Distribution curves showing the distribution of the Cs: K ratio and K content of some male members of the University of Toronto in 1959.

Naturally, considerable variation is present in the amount of K and Cs contained by normal people and this distribution is shown in Figure 4. The variation from person to person for the K mus is m ence cate amo ratio

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distribution depends on the amount of fat, muscle, etc. The variation of the Cs to K ratio is much broader and is due primarily to differences in diet. Studies by Marinelli9 have indicated that those people who consume a large amount of milk tend to have a larger Cs to K ratio. This tendency was confirmed in this study.

Caesium Content of Food

The Cs: K ratio of a number of foods collected during the spring of 1959 has been measured14 and some of the results are given in Table 1. It is seen that vegetables and fruits, in general, contain a relatively small amount of Cs whereas bread, beef and milk contain a relatively high amount of Cs. The second column of Table 1 gives an average daily intake of K13 and the last column gives the daily intake of Cs in µµC calculated from the figures of columns 1 and 2.

From the table it is seen that the estimated daily intake is 64 μμC of Cs137. Under equilibrium conditions, this figure multiplied by the biological mean lifetime of caesium in the body will give an estimate of the total caesium body burden. Assuming a biological half-life of 115 days5 and therefore a mean life of 166 days (115/0.693), one obtains a body burden of 1.1 x 10⁴ μμC. This is in reasonable agreement with the value found experimentally bearing in mind the fact that equilibrium conditions do not in fact obtain and that therefore the figure of 1.1 x 104 μμC is an upper limit.

Table I Spring 1959

Intake of Caesium-137 and Potassium

Product Group	Cs-K Ratio	Daily Potassium	Daily Caesium
	(C.U.)	Intake grams	Intake µµC
1. (i) Cauliflower	0 ± 6	0.78*	0.78*
(ii) Oranges Bananas	5 ± 5 0 ± 1	0.47	1.0
Bread	23 ± 6	0.22	5.1
2. Potatoes Carrots	$\begin{smallmatrix}0&\pm&2\\2&\pm&2\end{smallmatrix}$	0.41 0.78*	0.0 0.78*
3. Beef Fish	$ \begin{array}{c} 67 \pm 6 \\ 5 \pm 2 \end{array} $	0.40	21.8†
Milk	35 ± 3	1.0	35
		3.28	63.7

*From all vegetables except potatoes. Assumed that 1/5th of potassium intake from meat and fish is via fish.

Beta Dose

The dose arising from beta irradiation may be calculated from the relation

 $R_{\beta} = 51.2 \text{ C } \Sigma f_i \text{ E}_{\beta_i} \text{ rads/day}$ where C is the concentration in µc per gm and fi is the fraction of the beta disintegrations giving a mean beta energy of \mathbf{E}_{β_i} . The beta dose will be essentially uniform throughout the organ in which the isotope is concentrated except for a region of smaller dose at the surface of the organ. Cs and K are deposited mainly in muscle which constitutes nearly half the body (30 Kg out of 70 Kg). Since the muscle in turn is distributed over most of the body, it will be assumed, for purposes of dose calculation, that the ingested Cs and K are distributed uniformly throughout the whole body. If it were assumed that these isotopes were concentrated only in muscle and that the radiated energy was absorbed solely in the muscle, the calculated beta dose to the muscle would be larger by a factor of about 2. The average Cs content of the people tested was 8.4 x 10^{-3} µc yielding a concentration in the standard man (70 Kgm) of 1.2 x $10^{-7} \mu c/gm$. Summing $\Sigma f_i \to E_{\beta_i}$ for the beta rays from Cs¹³⁷, one obtains a dose of 0.59 mrads/yr.

The dose arising from beta rays of K⁴⁰ may be calculated assuming a person contains 140 gm of K and that $K^{(i)}$ occurs with a relative abundance of 0.0119% and decays with a half life of 1.25 x 109 yr. This gives a total K40 body activity of 120 x 10⁻³ µc, and a corresponding beta dose of 14.2 mrads/yr.

Gamma Dose

The calculation of the gamma dose from the two isotopes is more difficult because of the great range of the gamma rays. The gamma dose at any point P may be calculated from the relation

$$\begin{array}{ll} R_{\gamma_{_{\mathbf{p}}}} = & \int_{V} 10^{-3}. \; F.C.K. \; \frac{e^{-\mu r}}{r^2} dV \; \; rads/hr \\ = & 10^{-3} \; F.C.K. \; g_{_{\mathbf{p}}} \; rads/hr \end{array}$$

where K is the dose rate 1 cm from a 1 mc source in roentgens per hr, C is the concentration in μc per gm, f is the conversion factor from roentgens to rads and e-µr is the attenuation factor produced by r cm of tissue. The quantity gp is a geometric factor which has dimensions of length and is evaluated from the integral. Hine and Brownell¹¹ have calculated the average geometric factor \bar{g} for the whole subject and tabulated these values for subjects of different weights and heights. Since f is a slowly varying function with photon energy, a constant value of 0.96 may be used for it. The average gamma dose rate is then

$$R_{\gamma} = 23.0 \times 10^{-3} C K \overline{g} rads/day$$

Substituting $\bar{g} = 125$ for subjects 180 cm high and weight 70 Kg11 and K factors for Cs137 and K⁴⁰ of 3.1 and 0.82 r/hr/mc at 1 cm respectively, one obtains an average gamma dose rate of 0.39 mrads/yr for Cs137 and 1.49 mrads/yr for K40. These calculations are summarized in Table 2. It is seen that the average whole body dose from K40 is 15.7 mrads/yr and from Cs137 0.98 mrads/yr. It should be noted that the dose arising from K40 within the body is about 16 times that due to Cs137. From a casual examination of Figure 2 one might expect the two doses to be about the same since the peaks are about the same size. Indeed the doses from the gamma rays are much the same but because of the differences in the decay schemes, the beta doses are very different.

Table 2 — Dose per Year (millirads)

	β Dose	γ Dose	Total
K^{40} (120 x 10 ⁻³ μ c) Mean dose to whole body	14.2	1.49	15.7
Cs ¹³⁷ (8.4 x $10^{-3} \mu c$) Mean dose to whole body	0.59	0.39	0.98
Gonadal Dose from Natura Background (2)	al		95
Estimated Gonadal Dose from diagnostic procedures			
British (2)			21
American (4)			136

Discussion

For comparison, the gonadal doses arising from natural background (including K40) and from diagnostic procedures are given in Table 2. Strictly speaking, these cannot be compared with the mean body doses estimated for the K^{40} and Cs137 burdens but the average body doses from natural background and diagnostic procedures are probably not too different from the gonadal doses. From this table, it is clear that when the Cs137 body dose is compared with doses arising from K40 and other natural sources of the background, and with that arising from diagnostic procedures, the extra hazard presented by it is small. If, however, nuclear testing were continued over many years, it could create a real hazard, while a nuclear war would present a hazard of many orders higher magnitude.

ACKNOWLEDGMENTS: This work was supported by a Public Health Grant of the Department of National Health and Welfare and by the Department of Health of the Province of Ontario. The authors take pleasure in acknowledging the continued support of Dr. W. H. Watson, Head of the Department of Physics, University of Toronto; and to Mr. R. M. Green and Mr. O. A. D. Trojan for assistance in making these measurements.

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LOCALIZATION OF INTRACRANIAL LESIONS USING RADIOACTIVE IODINATED HUMAN SERUM ALBUMIN AND AN AUTOMATIC SCANNER

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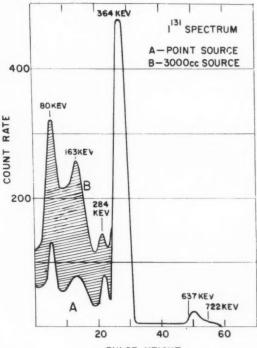
Saskatoon Cancer Clinic and Departments of Therapeutic Radiology and Neurosurgery, University of Saskatchewan, Saskatchewan.

The possibility of localizing an intracranial lesion by the external detection of gamma rays emitted from an intravenously injected radioactive isotope has much to commend it on the grounds of relative simplicity and the absence of the hazards inherent in anaesthesia and angiography. The fact that the procedure has not as yet become generally accepted in neurosurgical and neurological investigation may be attributed to lack of confidence, on the basis of published results purporting to show the 'accuracy of the method'.

Figure 1A

Unlike the other established special methods of investigation, including radiological contrast studies and electro-encephalography, there is, as yet, no single widely acceptable method utilizing radioactive isotopes. Instead, expressions of opinion as to accuracy of 'the method', varying from one out of twenty verified cases (Belcher et al.)1 through 46% (Seaman et al.)2 to 95% (Ashkenazy et al)3 must be viewed in the light of the many possible combinations of the following factors: (1) manual or automatic scanning; (2) the radioactive tracer used; (3) the nature and reliability of detecting equipment; (4) the method of data presentation and its intelligibility; (5) the inherent deficiency of rectilinear scanning in relation to the parasagittal region; and (6) the presence or absence of fore-knowledge of the likely or proved site of an intracranial lesion when interpreting the data.

Having found manual scanning of multiple areas of the head tedious and unrewarding, an automatic scanning device, technical details of which have been published elsewhere (Reid and Johns)4, was put into operation in April 1956 (Figure 1A)*. Neurosurgical evaluation of the method has been discussed elsewhere (Feindel et al.)7 and will be the subject of a separate report.



PULSE HEIGHT Figure 1B

In conjunction with this device the tracer used is RI131HSA (Abbott). Scanning with continuously moving detectors produces a record simultaneously of the distribution of both total radioactivity and differences in counting rate as seen from opposite sides of the skull.

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^{*}NOTE: In scans the head always appears to be viewed from the RIGHT.

Professor of Neurosurgery, McGill University and the Montreal Neurological Institute.

The device was designed so that both halves of the head would be scanned simultaneously, that the parasagittal regions would be included, and that the ends of the detectors would follow fairly closely the contour of an average adult skull, so that a more or less constant distance and geometry would be maintained. Briefly, the scanner has two similar detectors, each consisting of a 1 inch diameter, 1 inch thick, sodium iodide (thallium activated) crystal with associated photomultiplier, mounted in a 1 inch thick lead shield. Collimation is by a right cylinder, $\frac{3}{4}$ inch in diameter and $\frac{31}{4}$ inches long.

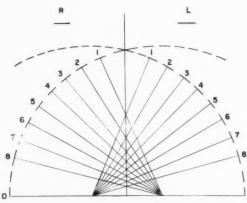


Figure 2. — Coronal section illustrating the crossfiring of the central axis of the detectors in each of the eight areas.

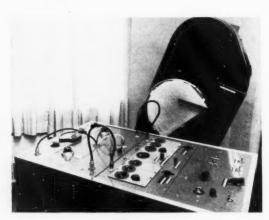


Figure 3

The detectors are mounted so that the head is scanned in a series of 8 parasagittal arcs, starting close to the nasion on the first run, each describing approximately 180°, and separated, in coronal section, by approximately 7½°. At the end of the scan the detectors are directly opposed, with their common axis in close relation to the tragus. Since both detectors follow fairly

closely the contour of the skull, their central axis is constantly focused on a vertical plane, which is $1\frac{1}{8}$ inch on the opposite side of the midline and close to the base of the skull. Figure 2 is a coronal section illustrating the crossfiring of the central axes of the detectors in each of the eight arcs. It follows that, at all times, both detectors are simultaneously 'seeing' a truncated cone of scalp, calvarium, brain, and base of skull. Because of this crossfiring of the central axes, or 'see-through', any focus of relatively increased radio-activity which lies deeply and fairly close to the midline may be recognized by both detectors at different times. In these circumstances, by triangulation, the most accurate localizations have been obtained. This prototype machine has the disadvantage of inflexibility, preventing the ipsilateral detector from 'seeing' the anterior temporal region. Measures to overcome this are being developed.

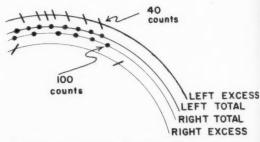


Figure 4 — Enlargement of a small segment of one arc with symbols. A dot represents a 100 counts. The oblique strokes represent an excess of 40 counts of one side over the other.

Technique

Adults receive 400 microcuries of RI131HSA intravenously, and on the same day are started on a three-day course of Lugol's iodine of 5 minims daily to block the thyroid. Depending on age and size, children are given lower doses, usually from 100 to 200 microcuries of RIHSA, and free iodide, either as Lugol's solution or potassium iodide solution. The above doses yield a counting rate of about 600 per minute, or 15,000 counts in the twenty-five minutes required to complete the scan. It is usual to scan approximately twenty-four hours after injection. Should there be any doubt as to interpretation, it is repeated either immediately or, more commonly, after a further twentyfour hours. A small series has been done both immediately and at twenty-four hours after injection.

The patient wears a rubber bathing cap, applied so as to present a smooth surface to the detectors, making symmetrical set-up easy, and preventing the head from slipping as it rests, extended, in the 1 inch wide plastic or leather

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ng cap, e to the asy, and it rests, leather sling seen in Figure 1. The head is centred and fixed by cushioned clamps applied to the malar eminences. The sling and clamp (Figure 1) are readily attached to a radiotherapy couch with provision for fine movement.

The patient's age, degree of consciousness, restlessness, and any tremor or rigidity have not constituted any problem in positioning.

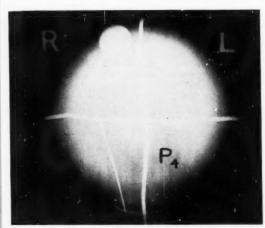


Figure 5A

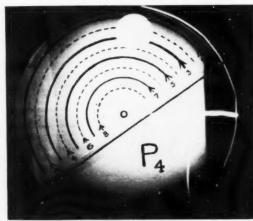


Figure 5B

A. P. and lateral views of Phantom (15 cm. flask containing NaI¹³¹ in water).

Once the head has been placed symmetrically between the detectors, these are moved to their starting position in the first parasagittal arc, close to the nasion. This position is shown on the paper scan by the simultaneous imprint of all four stampers and is usually denoted by the letter 'S'. At all times this starting point is close to the right hand short edge of the scintigram; the head, therefore, appears to be viewed from the right. The common axis of the detectors at the end of the scan is denoted by a small cross labelled 'O'.

Physical Basis of Method

All attempts at improving accuracy of localization are aimed, necessarily, at discrimination against the background of circulating radioactivity. Decreasing size and increasing depth of the lesion, and a low ratio (tumour/normal tissue) of specific radioactivity, make the problem of detection more difficult.

The present method minimizes the problem of background in two ways, as follows: (1) since it is assumed that background radiation is essentially homogeneous and equal from both halves of the head, differences in radioactivity of identical volumes are recorded; (2) all photons of energy below approximately 300 Kev are disregarded. This lower energy limit allows recognition of small-angle scattering of the 364 Kev photons from I131, as well as of the small contribution from more energetic photons. It eliminates the less energetic ones which, in a scattering medium, account for approximately two-thirds of the total energy loss and serve merely to accentuate the presence of the woods while obscuring the detail of the trees.

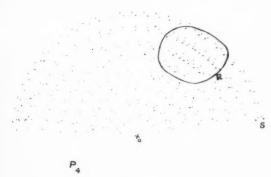


Figure 6

Figure 1B represents the spectral distribution of gamma rays from I^{131} as a point source in air(A) and as a large source in a scattering medium(B), such as obtains in the skull.

Since two similar, but not necessarily identical, circuits are involved, the spectrum in a scattering medium has to be determined separately for each detecting system, and, in order to discriminate equally on both sides, discriminator settings have to be individually adjusted. Since the data recorded represent not only the total radioactivity, but also differences in intensity of radioactivity as seen by both detectors simultaneously, it is imperative that the two detecting systems be 'balanced' carefully both before and after each scan. This is done by placing a 3 litre, 15 cm. diameter glass flask containing a solution of some 12 to 20 microcuries of NaI¹³¹ symmetrically between

the directly opposed collimators. Differences in counting rate should not be greater than 1% in approximately 10,000 counts recorded by each detector. Checking for imbalance at the end of a scan takes but a few minutes and is important in determining the validity of the recorded data.

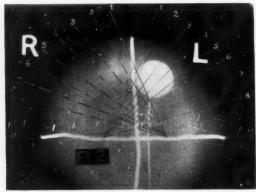
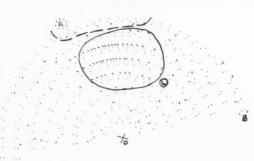


Figure 7



P2

Figure 8

Data Presentation

Data are recorded by printing four different sets of symbols on 'Tracergram' paper using mechanically activated steel stampers which oscillate with the same angular and linear velocity as the detectors. The flat paper is carried on a stationary circular aluminum platform, whose centre is on the common axis of the detectors (Figure 3). The 'scan' or 'scintigram' is in the form of eight concentric arcs corresponding with the parasagittal arcs described by the detectors. To maintain uniform density of the stamped data from a source of uniform radioactivity, linear velocity of the detectors and stampers is kept constant by increasing angular velocity automatically as the radius of each arc decreases. Figure 4 illustrates the symbols stamped, their significance and their relative position in a small segment of any one arc. They consist of dots and oblique strokes. Each dot represents 100 counts, the upper (or outer) row recording the total radioactivity in terms of photons of energy 300 Kev and above, as 'seen' by the left detector. Similarly, the lower (or inner) row of dots represents the total radioactivity seen by the right detector throughout the same interval and from a symmetrical volume of the head. The oblique strokes are a measure of the difference in intensity of radioactivity presented to the individual detectors during the same short interval. Each oblique stroke in the upper (or outer) row denotes a difference of 40 counts of Left over Right. When the right detector is 40 counts ahead of the left, an oblique stroke will appear on the lower (or inner) row. This number is arbitrary, but was found by trial to give the most satisfactory scans.

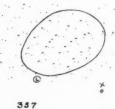


Figure 9 Scan 357 — Left parieto-temporal infarct demonstrated at autopsy.

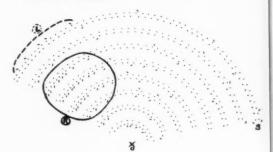




Figure 10 Partial scan 315 — Recurrent right temporoparietal Astrocytoma, Grade IV, 7 months postoperatively. Note 'see-through' in same sector of different arcs.

Apart from random strokes, more gross local changes may appear on one particular arc of the scintigram (e.g. from the transverse sinus) and for this reason only a definite pattern of increased radioactivity in the same sector of several arcs may be regarded as evidence of localization.

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Interpretation of scans:

All scans have been interpreted by one of the first two authors, (usually GABC) and an active attempt has been made to know nothing about the patient's symptoms and signs. Almost invariably the test precedes all other special investigations.

For a scan to be considered reliable, the counting rate should be of the order 600 per minute and the balance, both before and after, should be within 1%.

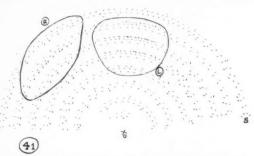


Figure 11 Scan 41—Two separate lesions: one left posterior frontal; the other, right parietal. As these are in different sectors of the same arcs, 'seethrough' is excluded. Lesion on left was found to be a pyogenic abscess (actinomycosis). At autopsy, some weeks later, a smaller abscess was found in the right parietal cortex.

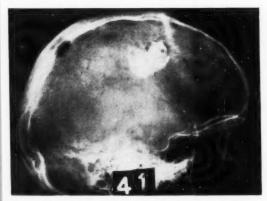


Figure 12 — Thorotrast in left posterior frontal abscess cavity of same patient as in Figure 11.

In the event that a focus of increased radioactivity is localized, it will appear on the scan as a pattern of strokes and dots on more than one arc on one or both 'sides' of the scan. For any given small focus, the nearer it is to the surface, the more dense will be the oblique strokes on that 'side' of the scan and the more sharply demarcated will be the edges of the pattern of increased radioactivity. Figure 5A and Figure 5B are antero-posterior and lateral views of a phantom (P_4). This is a 15 cm. diameter 3 litre flask containing 20 μc NaI¹³¹

in water. The 'tumour', a Foley catheter, containing 1 μc of NaI in 15 cc of water is placed to simulate a lesion in the right frontal parasagittal area. The ratio of specific activities (tumour/background) in thus 10:1. Figure 6 shows the 'scan' obtained. For the same focus lying more deeply, the pattern of oblique strokes will be less intense and will be spread over a slightly larger segment of the same, and perhaps one or two extra arcs. If now the same focus lies close to the midline, it will be seen by both detectors at different times, and will produce a pattern of strokes and dots on both 'sides' of the scan. The detector nearer to the focus will produce a denser pattern of oblique strokes in a smaller segment of more arcs than will the other, which, being further away, will see the focus throughout a greater part of its traverse on only one or two different arcs (Figures 7 and 8, Phantom P_2).

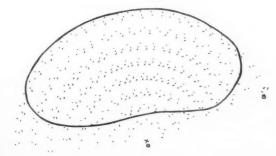


Figure 13 Scan 159 — Right fronto-parietal chronic subdural haematoma.

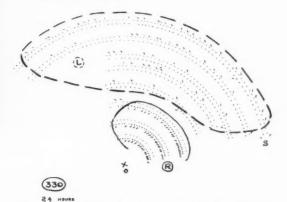


Figure 14 Scan 330 — Partial scan of large right temporal astrocytoma.

Note 'see-through', showing that lesion extends very deeply.

Results

Table 1 summarizes the distribution of the results of scanning 281 patients. Although there were 436 scans, only one relevant scan is

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arc of e sinus) etern of ector of ence of counted per patient. This large excess of total scans over total patients is due to several factors, namely; repeat scanning at various intervals prior to, and following, surgery; an experimental series of scans both immediately after injection and at 24 hours; repetition of scans using different collimators and of others considered technically unsatisfactory due to either mechanical or electronic faults; and repetition at approximately 48 hours of scans which at 24 hours were of doubtful significance or, being frankly positive, were repeated in order to determine accuracy of reproduction.

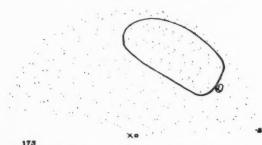


Figure 15 Scan 173 — Left posterior frontal parasagittal astrocytoma, Grade III, with a single large cyst, in a child aged 41/2 years.

We believe that if the accuracy of automatic brain scanning with radioactive isotopes is to be fairly assessed, the scintigrams must be interpreted at their face value, without any knowledge of the likely or proved site of an intracranial lesion. Such knowledge almost inevitably, in our opinion, will cause bias when interpreting a scan which is doubtfully positive and we feel that, in such cases, the doubt should be resolved by repeating the scan either immediately or next day. We have not designated any scans 'doubtfully positive' or 'doubtfully negative'. A small number of scans (26) has been discarded, 'unclassified', as subsequently defined. These discards occurred early in the series before we appreciated the supreme importance of careful discriminator setting.

The following is a list of the terms used in this study, and their definition.

Verified: Positive diagnosis or localization by more than one of the following: x-ray of skull, pneumography or ventriculography, cerebral angiography, surgical exploration, biopsy or autopsy.

Unverified: Having had no, or inadequate investigation by accepted methods as listed above.

True Positive: Scans showing a definite localization substantiated by contrast studies and verified by surgical exploration with biopsy and with or without (in one case only) histological proof.

True Negative: Scans showing no localization, substantiated by negative X-ray of skull and contrast studies.

False Positive: Scans showing a definite localization proved to be false by contrast studies showing no evidence of localization.

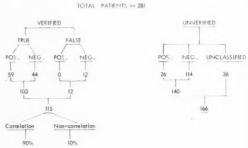
False Negative: Scans showing no localization, whereas a lesion was demonstrated by contrast studies and operation with or without histological proof.

Unverified Positive: Scans showing a definite localization but without sufficient other investigation to determine whether they are true or false positives.

Unverified Negative: Scans showing no localization but without adequate further investigation.

Unclassified: (a) Scans which are either technically unsatisfactory, doubtfully positive, or doubtfully negative which have not been repeated, and for which there is no other corroborating or contradictory evidence; (b) scans which have changed from negative to positive over a prolonged period (many weeks or months), without verification.

Table 1 SASKATOON AUTOMATIC BRAIN SCANNER April 2, 1956 ----- December 31, 1958



It will be noted in Table 1 that verification of the results of automatic scanning has been obtained in 115 patients and that of these 59 have been verified as 'true positive' as defined above. In only one instance, that of a young boy, was no histological proof obtained of what was considered at surgery to be a thalamic glioma. It is significant that there has not been a single verified false positive scan, if the 26 'unclassified' scans are excluded. There were, however, 26 'unverified positive' scans.

Table 2 lists the various types of lesion localized and their numerical distribution. Table 3 shows the nature and location of lesions responsible for the twelve false negative scars. 101 Vol.

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Cowan et al: Localization of Intracranial Lesions

Discussion

Manual scanning of multiple symmetrical areas of the skull with a single open-ended detector has little to commend it. Alternative techniques to increase accuracy of localization utilize, almost exclusively, automatic scanning devices. An exception is the graphic analysis method of Chou and French⁵, who record an accuracy of localization of 87% in 69 patients, compared with 68% by the usual method of asymmetry.

Table 2

Table 3

FALSE NEGATIVES

LESIONS CONFIRMED BUT NOT LOCALISED

TOTAL 12 PATIENTS

ASTROCYTOMA GRADE 1811 5*

GRADE III 8.IV
(L.OCCIPITO-PARIETAL)

MEDULLOBLASTOMA 1

CHROMOPHOBE ADENOMA 4

CONGENITAL ARACHNOID CYST

*ONE EACH IN:
FRONTO-TEMPORAL REGION
OCCIPITAL LOBE
BRAIN STEM
IIIrd VENTRICLE
POST. IVIN VENTRICLE

(L.FRONTO-TEMPORAL)

Rectilinear scanning, which is mechanically relatively simple, has the following inherent defects: (a) the skull must be scanned in more than one projection; (b) the immediate parasagittal region is at a great distance from the

detector(s) in lateral projection, thus reducing the chance of finding a small focus in this zone, in close proximity to the high background of the sagittal sinus. Attempts to improve resolution with rectilinear scanning involve the use of a large crystal for increased efficiency, and a multichannel focussed collimator. This combination is both costly and bulky, due to the shielding required.

While rectilinear scanning by two opposed detectors is a *sine qua non* of positron-emitting, the two most commonly used have particular disadvantages: (a) Arsenic⁷⁴, being cyclotron-produced, is not readily available; (b) Copper⁶⁴ versenate has a very short half life (12.8 hours) so that, in the interests of economy, patients must be scanned in groups, on the day following shipment of the tracer. The test is thus not available on demand, and therefore becomes an elective procedure. Repeat scanning is restricted by the short half life and the large dose (up to 3 mc) necessary for adequate initial counting rates.

The present method overcomes the above disadvantages by utilizing the readily available tracer RI¹³¹HSA, the physical half life of which (8.05 days) allows scanning from a single dose to be repeated at up to 4 to 5 days. The test can be done on demand, is inexpensive and, with thyroid blocking, involves the patient in little radiation hazard.

The short time required to complete the test improves its usefulness.

In assessing the value of a method such as this, involving clinical material, two factors have to be remembered: (1) we are not dealing with an exact science; (2) the method has to be judged on the basis of other special investigations which in themselves are not uniformly unequivocal.

Consequently, we feel that the expression '% accuracy' is meaningless at this stage, and that all that can be stated is the degree of correlation between the new method and those others constituting the yardstick by which it is measured.

While it is agreed with Harris⁶ that increased resolving power of the present detectors is possible, we feel that any theoretical advantages would be far outweighed by the following practical considerations: (1) the much larger diameter crystals and shielding required would produce undue separation of the detectors on the first parasagittal arc, thereby removing one of the major advantages of the system; (2) if multichannel focussed collimators were substituted, expense and scanning time would be increased; (3) it seems unlikely that much improvement in the degree of correlation shown could be obtained.

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bution. lesions scans. Experiments have, however, been started using tapered collimators and, in order to increase efficiency, it is proposed to substitute longer crystals.

Summary

Our experience with an automatic brain scanning device in a series of 281 patients over a period of some $2\frac{1}{2}$ years has been described.

It is suggested that this method has certain advantages over others currently in use.

On the basis of careful assessment of the scans in 115 verified cases, good or excellent correlation has been obtained in 90% with failure of localization in the remaining 10%. There have been no verified 'false positive' scans. There were 26 'unverified positive scans' and 26 scans considered as 'unclassified'.

The procedure is simple and rapid, available on demand, not hazardous, and is easily repeated. The test is thus of value in 'screening' certain neurosurgical and neurological problems, in post-operative follow-up, and, when positive, as an indication for further special investigation.

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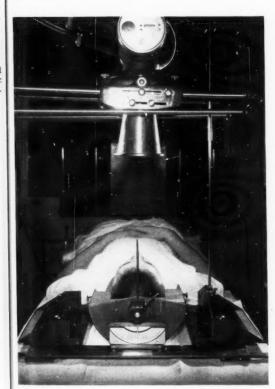
A NEW DEVICE FOR SKULL RADIOGRAPHY

W. RENNER, M.D.

Hotel Dieu Hospital, Cornwall, Ontario.

Radiology of the skull and brain has grown into a sub-specialty within radiology during the last two decades. A considerable amount of knowledge has been accumulated in the interpretation of findings in skull films but much depends on the experience, skill and accuracy of the technician who takes the films.

A device to standardize skull radiography has been developed.



Three conditions had to be fulfilled:

- 1) The patient's head had to be immobilized in a position which could be maintained until the examination was completed.
- 2) The immobilization had to be so comfortable that even an irrational patient would not try to move his head.
- 3) The immobilization device had to be flexible enough to permit all standard and special views of the skull.

The existing head clamps and positioning devices certainly do not fulfil these conditions, and they are seldom used by some radiographers.

The difference in the size and shape of skulls of patients over 2 years of age is negligible from the immobilization point of view. This is clearly shown by the fact that most exposure charts neglect individual measuring for skull radiography.

Foam plastic provides sufficient elasticity to keep the head in a comfortable position regardless of size or shape, and does not cast undesirable shadows. Five different foam plastic head supports were made for: (1) AP, (2) PA, (3) Right lateral, (4) Left lateral, (5) Water's projection. These are called inserts in the text.

Two foam plastic straps at the forehead and chin help to secure immobilization for restless patients. The foam plastic can be washed and sterilized. All inserts provide for breathing space. These foam plastic inserts are put into an aluminum shell, the longitudinal axis of which coincides with that of the Bucky table. With the patient in the supine or prone position, the head can be rotated around the longitudinal axis which is pivoted at the level of the average sella turcica. The shell and insert can be locked at any angle up to 45° on either side. A metal bar and pointer-bar serve the purpose of proper alignment in the cranio-caudal and transverse axis. This bar can be turned to either side without interference with the position of the head. All rotations of the patient's head in the apparatus are in the longitudinal axis. No motion of the X-ray tube will be required that could interfere with the longitudinal centering of the Bucky grid. All films are to be taken with an FFD of 40". A second angligner is attached to the apparatus at the side of the patient's head. This angligner is also pivoted at the level of the sella turcica. It can be moved to either side of the patient's head and has a telescopic extension which is graded in a way that the distance of 40" between the film in the Bucky and the focal spot will be kept constant. This helps to overcome the sometimes not negligible inaccuracy of the scales which measure the angulation of the cranial or caudal tilt of the tube head of X-ray machines. A scale on the side of the apparatus can be drawn out over the side of the table top. On this scale there are marks to indicate where the centre of the cassette in the Bucky has to be, to obtain a radiograph which does not cut off parts of the skull. In the series of films which

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B., and tomatic Ibumin. have been taken in this hospital a film size 10" x 12" was used. 8" x 10" sized films can also be used. Included on this scale and opposite each angle center point, is a scale which reads the exact distance from the perpendicular on the tube stand to give the required 40" FFD.



The lateral angligners are easily removed. A $10^{\prime\prime}$ x $12^{\prime\prime}$ cassette fits into the adjustable slots for purpose of lateral views in the supine position. This proved to be of great value in accident cases at night when the patient could not turn into the prone position and only one radiographer was available.

The moving parts of this unit are mounted on a base plate of aluminum which can be attached to any radiographic table so that the centre coincides with the midline of the table. It is easily handled as it only weighs 12 lbs. This attachment is so compact that the table can be turned into an upright position and the apparatus will not slide. This makes it possible to take films of the paranasal sinuses in the upright position. The common practice of taking the first films during an encephalography in the upright position to obtain optimal visualization of the 3rd and 4th ventricles is also facilitated by this device.

Carotid and vertebral angiograms can be easily obtained with this device, as there is practically no danger of voluntary or involuntary movement of the patient. Stereoscopic skull films and tomograms depend on perfect immobilization of the skull in the examination of very often uncooperative patients. The use of the foam plastic straps is seldom necessary because of the psychological effects of comfort the patient feels in the inserts. Even babies are usually quiet, but special inserts for babies can be made.



It was found that the usefulness of this unit was not limited to skull radiography. By resting and immobilizing the patient's head in a comfortable position it was much easier to do Tomographic examinations of the chest, as it is nearly impossible to move the chest while the head is fixed. The absorption of radiation by the polyurethane inserts is negligible in the range of exposures normally used for skull radiography. If anything, they reduce the undesirable contrast in the periphery of the skull. The magnification factor over the conventional method is negligible. It is obvious that the advantages of coning down are neither overcome by the inserts nor by the aluminum shell. If the aluminum shell has a thickness of 1/8 inch. the skin dosage to the patient only increases by 1 r with 10 exposures. JO Vol.

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As the position of the skull does not in all cases coincide with the recommended routine radiographic positions, sets of films are prepared to show how tilting of the table and rotation of the patient's head affect the visualized anatomy. This was done after we found out that some of the conventional positions of the head are not only difficult to maintain without support (Caldwell's position) but even with support. After accumulating a certain amount of experience it was found that the films obtained with this immobilization device were so uniform in quality that an attempt at standardization could be made. A wall chart for the radiographic room was prepared and all positions were numbered. A radiologist's desk chart will be made (a miniature replica of the wall chart), so that the radiologist can establish the routine views he wants and ask for additional views according to their number on the chart. It was found that even the student technicians could produce good skull work. They did not have to worry about distance, centering, exposure and possible movement of the patient. Nobody had to hold the patient's skull and repeat examinations were rarely necessary. The average time for a skull examination was cut in half.

Summary

A skull immobilizing and positioning device was developed which permits standardization of skull radiography. With this device even an inexperienced technician can take skull films in half the time which would be normally required. The patient's head rests firmly and comfortably in foam plastic holders, which are designed for the different positions of the skull. Additional features permit a constant FFD, accurate centering and accurate angulation. The device especially facilitates skull radiography on restless and comatose patients, stereoscopic views, angiograms and tomograms.

We hope that this device will enable radiographers in small country hospitals to produce skull films comparable to those made in the larger hospitals.

Similar devices for standardization of radiography of other parts of the human body have been investigated with promising results.

ACKNOWLEDGMENT: Mr. R. K. Travis, the Rev. Sister A. Callagher and the advice of Dr. A. Halloway, Kingston.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Radiologic Examination of Small Intestine, by Ross Golden, M.D., D.Sc., The Ryerson Press, Toronto,

Cinefluorography, Edited by George H. S. Ramsey, M.D., James S. Watson, Jr., M.D., Theodore A. Tristan, M.D., Sydney Weinberg and William S. Cornwell, M.A., Ryerson Press, Toronto, \$13.00.

THE CANADIAN ASSOCIATION OF RADIOLOGISTS

A Meeting of Council will be held at the Banff Springs Hotel, June 11th and 12th, 1960.

VITH SYMPOSIUM NEURORADIOLOGICUM — ROME

The VIth Symposium Neuroradiologicum will be held in Rome, September 18-22, 1961, under the Presidency of Dr. Giovanni Ruggiero. All correspondence should be addressed to Dr. Enzo Valentino, General Secretary, VIth Symposium Neuroradiologicum, CIT — Ufficio Congressi - p. Colonna 193, Rome, Italy.

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